Evidence Report/Technology Assessment
Number 75

Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cancer

Agency for Healthcare Research and Quality

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. Endorsement by the Agency for Healthcare Research and Quality (AHRQ) or the U.S. Department of Health and Human Services (DHHS) of such derivative products may not be stated or implied.

AHRQ is the lead Federal agency charged with supporting research designed to improve the quality of health care, reduce its cost, address patient safety and medical errors, and broaden access to essential services. AHRQ sponsors and conducts research that provides evidence-based information on health care outcomes; quality; and cost, use, and access. The information helps heath care decisionmakers—patients and clinicians, health system leaders, and policymakers—make more informed decisions and improve the quality of health care services.

Evidence Report/Technology Assessment

Number 75

Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cancer

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
http://www.ahrq.gov

Contract No. 290-97-0001

Prepared by:
Southern California Evidence-based Practice Center
Paul Shekelle, MD, PhD
EPC Director

Ian Coulter, PhD
Mary Hardy
Principal Investigators

Sally C. Morton, PhD
EPC Co-Director/Senior Statistician

Jay Udani, MD
Myles Spar, MPH, MD
Karen Oda, MD
Lara K. Jungvig, BA
Wenli Tu, MS
Roberta Shanman, MLS
Sydne Newberry, PhD
Louis R. Ramirez, BA
Di Valentine, JD
Investigators

AHRQ Publication No. AHRQ 03-E047
August 2003

ISBN: 1-58736-091-5

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Suite 6000, Rockville, MD 20850.

Carolyn Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean R. Slutsky, P.A., M.S.P.H.
Acting Director
Center for Practice and Technology Assessment
Agency for Healthcare Research and Quality

Structured Abstract

Objectives. The objective of this report was to conduct a comprehensive literature review and synthesis of evidence on the use of the supplements vitamin C, vitamin E, and coenzyme Q10 for the treatment and prevention of cancer.

Search Strategy. We performed a search of 13 databases through early 2001 using the terms coenzyme Q10, vitamin C, and vitamin E and their many pharmacological synonyms. The bibliographies of review articles were also searched, and experts were questioned to identify additional citations.

Selection Criteria. Reports were included in the synthesis of evidence if they focused on the use of supplements of coenzyme Q10, vitamin C, or vitamin E for the prevention and treatment of cancer and presented the results of clinical trials on human subjects. Language of publication was not a barrier to inclusion.

Data Collection and Analysis. All selected titles, abstracts, and articles, in all languages, were reviewed independently by two reviewers fluent in the appropriate language. Information was collected about patient demographics, disease state, intervention, study design, and outcomes. We focused on three primary outcomes: death, development of new tumors, and effect on colonic polyps. For deaths and new tumors, the trials were too heterogeneous to pool for meta-analyses. For colonic polyps, the trials were sufficiently homogeneous to support a meta-analysis.

We also identified a group of trials with intermediate outcomes, and these were reviewed in a qualitative analysis.

Main Results. We identified 432 articles for screening from which 35 articles met the criteria for inclusion in the analysis. These articles represented 37 unique studies and 22 unique trials, because many studies presented data on the same trial. The identified trials varied greatly in quality. For the doses and populations studied in the trials.

- There was no evidence found for assessing the efficacy of coenzyme Q10 for prevention or treatment of cancer.
- We identified three large trials assessing the effect of vitamin C and vitamin E in various combinations given to persons without cancer. No trial reported a statistically significant beneficial effect on death due to cancer. Subgroup analysis did identify a statistically significant 9% reduction in all cause mortality and a borderline significant 13% reduction in all-cancer mortality associated with supplemental vitamin E in combination with other micro-nutrients. All other trials showed no benefit for all other types of new tumor development except for one arm of the ATBC trial, which showed a decrease in the development of new prostate tumors.
- We identified seven trials that assessed the use of vitamin C in patients with advanced cancer. No trial reported a statistically significant mortality benefit.
- There was no decrease in risk of death for vitamin C as a treatment for advanced cancer.

- We identified six trials assessing the effect of combinations of vitamin C and vitamin E with and without beta-carotene on the development of colonic polyps. No trial reported a statistically significant beneficial effect.
- We identified six unique trials that reported on various intermediate outcomes.
- The following beneficial results were reported from single trials:
- a. Vitamin C was found to be beneficial in reducing the occurrence of new tumors in a single trial of patients with bladder cancer also treated with bacillus Calmetee-Guerin (BCG).
- Vitamin E in combination with omega-3 fatty acid increases survival in patients severely ill with a variety of malignancies.
- A number of intermediate outcomes studies were positive.

Conclusions. For the interventions tested, in the populations described, there is scant evidence that vitamin C or vitamin E beneficially affects survival. Similarly, for the interventions tested, in the populations described, there are no results suggesting a benefit for the prevention of new tumors, which reach statistical significance with the exception of prostate cancer in subjects treated with alpha-tocopherol. One trial reported a benefit of a megadose vitamin therapy on the development of new tumors in patients with bladder cancer. However, the ability to infer from this finding is limited because the multi-component intervention limits our ability to attribute the reported efficacy to any particular component.

For the outcome for colonic polyps, four trials focusing on secondary polyp recurrence could be pooled for analysis and none used vitamins C or E as a single intervention. The combination of vitamins C and E was not clinically superior to placebo in secondary prevention. The combination of vitamins C and E with beta-carotene or vitamin A did show a trend favoring a reduction in polyp recurrence, but this finding was not statistically significant.

The systematic review of the literature does not support the hypothesis that the use of supplements of vitamin C or E or coenzyme Q10 generally help prevent and/or treat cancer. There were isolated findings of benefit, which require confirmation.

Future Research. Future research should be done to confirm the positive findings from the single trials identified here. Investigation should be undertaken to understand the discrepancy between the epidemiologic evidence and the clinical trial data. Additional research should include population (such as women) not well studied.

Suggested Citation:
Coulter I, Hardy M, Shekelle P, et al. Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cancer. Evidence Report/Technology Assessment Number 75. (Prepared by Southern California Evidence-based Practice Center under Contract No. 290-97-0001.) AHRQ Publication No. 03-E047. Rockville, MD: Agency for Healthcare Research and Quality. August 2003.

Contents